by deleting the bracketed material and inserting the underlined material as follows:

--1. (2X Amended) An antibody which specifically binds to human luteinizing hormone beta core fragment (hLHβcf) without cross-reacting with human luteinizing hormone (hLH), human luteinizing hormone free beta subunit (hLHβ) or human chorionic gonadotropin beta core fragment (hCGβcf), which antibody binds to the same epitope on human luteinizing hormone beta core fragment as an antibody produced by hybridoma cell line designated B505 (ATCC Accession No. HB-12000).--

**REMARKS**

Claims 1 and 4 are pending in the subject application. Applicants have hereinabove amended claim 1. Support for these amendments may be found inter alia in the specification as follows: page 1, lines 20-31; page 14, lines 16-21. This amendment does not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 1 and 4 will be pending.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 1 and 4 under 35 U.S.C. §103(a) as being unpatentable over O'Connor et al. (*Endocrine Reviews 15(6):650-683, 1994*) in view of Campbell (Monoclonal Antibody Technology, Elsevier Sci.Publishing, 1984) for the same reasons set forth in Paper No. 4, dated 9/13/00.

The Examiner stated that applicant's arguments, filed 3/16/01(Paper

No. 5), have been fully considered but are not found persuasive. The Examiner stated that applicant argues that the O'Connor et al. reference does not teach the invention of claims 1, i.e. an "antibody which specifically binds to human luteinizing hormone beta core fragment(hLHβcf) without cross reacting with hLH, hLhβ or hCGβcf. The Examiner stated that applicant's further submit that O'Connor et al does not teach, suggest or disclose the human luteinizing hormone free beta subunit. The Examiner stated that applicant's further state that the secondary reference, Campbell, is a general reference regarding the synthesis of monoclonal antibodies which does not teach, suggest or disclose human luteinizing hormone free beta subunit. The Examiner stated that in addition, applicant's note that the O'Connor et al. reference states that the production of "monoclonal antibodies specific for hCG, as compared to the highly homologous hLH has not been a straightforward process"and there would not have been a reasonable expectation of success in making the claimed antibody specific for one but not the other molecule, such as hCG but not hLH.

The Examiner stated that however, the Examiner notes that O'Connor et al. does not describe antibodies synthesized specifically agains the human luteinizing hormone beta core fragment but does describe the (antigens) structural similarity and dissimilarities between the hCG, hCG β, hCG β-core fragment, hLH, hLHβ, and the hLH β-core fragment(the β core fragment being homologous proteolytically cleaved fragments of the β subunit of hCG or hLH) and the difficulty in obtaining antigen-specific sera between the members (see page 654, column 2 and page 657 column 2 to 658 column 1 in particular). The Examiner stated that O'Connor et al. note the identity between the α subunits of the family members and how they

differ primarily in their β subunits(see page 650, column 2 in particular). The Examiner stated that O'Connor et al. further describe their isolation of the hLHβ core fragment which isunique from the hLHβ as it lacks some of the internal sequences of the β subunit of hLH. The Examiner stated that O'Connor further note the amino acid identity between the hLH β core fragment at the amino terminus but its apparent dissimilarity between the two. The Examiner stated that O'Connor note the use of this unique COOH terminus in hCG to generate antisera to eliminate the problem of cross-reactivity with hLH. The Examiner stated that finally O'Connor et al. note that although producing monoclonal antibodies which differentiate between hCG and hLH has not been straightforward, monoclonal antibodies could be screened and selected for specificity because of the unique capability of monoclonal antibody technology. The Examiner stated that O'Connor further note that subsequent screening yielded an antibody with high affinity to hCG and free hCG β-subunit but not the hLH or its β-subunit(see page 659, column 2 in particular).

The Examiner stated that consequently O'Connor et al. teach the structural similarity between hCG, hCGβ, hCG β-core fragment, hLH, hLHβ, and hLH β-core fragment and how this similarity leads to problems with immunological cross-reactivity. The Examiner stated that the major structural dissimilarity in the β-subunits between these family members is at the COOH terminus which can be exploited to generate hCG-specific antisera.

In response, applicants respectfully traverse the Examiner's above rejection. The cited references, namely O'Connor et al in view of Campbell et al. do not render obvious the claimed invention.

Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have herein amended claim 1. Newly amended claim 1 recites an antibody which specifically binds to human luteinizing hormone beta core fragment (hLHβcf) without cross-reacting with human luteinizing hormone (hLH), human luteinizing hormone free beta subunit (hLHβ) or human chorionic gonadotropin beta core fragment (hCGβcf), **which antibody binds to the same epitope on human luteinizing hormone beta core fragment as an antibody produced by hybridoma cell line designated B505 (ATCC Accession No. HB-12000)** [emphasis added]. Applicants contend that the cited references do not teach, suggest or disclose such an antibody. Neither of the cited references disclose an antibody produced by hybridoma cell line B505 (ATCC Accession no. HB-12000). Accordingly, neither reference could nor does suggest an antibody which binds to the same epitope on hLHβcf as the B505 antibody, while also not cross-reacting with hLH, hLHβ or hCGβcf. Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Summary

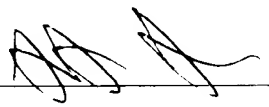
For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims, i.e. claims 1 and 4.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone either of them at the

number provided below.

No fee, other than the enclosed $460.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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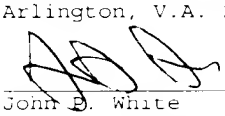
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 2327, Arlington, V.A. 22202



12-4-01

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**Exhibit A**

--1. (2X Amended) An antibody which specifically binds to human luteinizing hormone beta core fragment[,] (hLHβcf) without cross-reacting with human luteinizing hormone (hLH), human luteinizing hormone free beta subunit (hLHβ) or human chorionic gonadotropin beta core fragment (hCGβcf), which antibody binds to the same epitope on human luteinizing hormone beta core fragment as an antibody produced by hybridoma cell line designated B505 (ATCC Accession No. HB-12000).--